Phosphorus flame retardants in indoor dust and their relation to asthma and allergies of inhabitants

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Abstract

Organophosphate esters are used as additives in flame retardants and plasticizers, and they are ubiquitous in the indoor environment. Phosphorus flame retardants (PFRs) are present in residential dust, but few epidemiological studies have assessed their impact on human health. We measured the levels of 11 PFRs in indoor floor dust and multi-surface dust in 182 single-family dwellings in Japan. We evaluated their correlations with asthma and allergies of the inhabitants. Tris(2-butoxyethyl) phosphate was detected in all samples (median value: 580 μg/g in floor dust, 111 μg/g in multi-surface dust). Tris(2-chloro-*iso*-propyl) phosphate (TCIPP) was detected at 8.69 μg/g in floor dust and 25.8 μg/g in multi-surface dust. After adjustment for potential confounders, significant associations were found between the prevalence of atopic dermatitis and the presence of TCIPP and tris(1,3-dichloro-2-propyl) phosphate in floor dust (per $\log_{10}$-unit, odds ratio: 2.43 and 1.84, respectively). Tributyl phosphate was significantly associated with the prevalence of asthma (odds ratio: 2.85 in floor dust, 5.34 in multi-surface dust) and allergic rhinitis (odds ratio: 2.55 in multi-surface dust). PFR levels in Japan were high compared with values reported previously for Europe, Asia-Pacific, and the USA. Higher levels of PFRs in house dust were related to the inhabitants' health status.

Key words

phosphorus flame retardants (PFR)

organophosphate triesters

indoor dust

dwellings

asthma

allergy

Practical implications

Organophosphate esters are used as an alternative for polybrominated diphenyl ethers. Phosphorus flame retardants (PFRs) are categorized as semi-volatile organic compounds (boiling point, >250°C), and many PFRs are not chemically bonded to the final products and can easily be released into the indoor environment. This study provides information on the levels of PFRs in house dust in Japan and shows positive correlations between the prevalence of asthma and allergies and the presence of PFRs. The results indicate the importance of monitoring PFRs in house dust to determine their effects on asthma and allergies and whether they may have a causative role in these illnesses.

Introduction

People in modern society are routinely exposed to many different man-made chemicals. One such class of chemicals is the organophosphate esters, which are used as additives in flame retardants and plasticizers and are found in a variety of products. In 2003, the European Union banned the use of two classes of flame retardants, polybrominated diphenyl ethers (PBDEs) and polybrominated biphenyls, and their use has voluntarily decreased in the USA as well (van der Veen and De Boer, 2012). As a result of the restrictions on the use of PBDEs, the use of organophosphate flame retardants (PFRs) as an alternative flame retardant additive is increasing (Bergman et al., 2012; Le Cann et al., 2011). Polyurethane foam, thermoplastics, resins, polyvinylchloride, synthetic rubbers, and textiles are major products that contain tributyl phosphate (TNBP; CAS number 126-73-8), tris(2-chloroethyl) phosphate (TCEP; 115-96-8), tris(2-chloro-*iso*-propyl) phosphate (TCIPP; 13674-84-5), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP; 13674-87-8), and triphenyl phosphate (TPHP; 115-86-6) (Stapleton et al., 2009; van den Eede et al., 2011). TCEP, TCIPP, and TDCIPP are used as replacements for penta-BDE (Dodson et al., 2012). TNBP, TPHP, and tricresyl phosphate (TMPP; 1330-78-5) are also used as lubricants, and tris(2-butoxyethyl) phosphate (TBOEP; 78-51-3) is often used in floor wax (WHO, 2000). Indoor sources of PFRs include furniture, bedclothes, electronics, interior surfaces (such as walls, ceilings, and floors), and baby products (such as car seats, mattresses, nursing pillows) (Saito et al., 2007;

Stapleton et al., 2009).

The presence of PFRs in indoor dust has been reported in Europe (Belgium, Germany, Romania, Spain, and Sweden), the USA, and Asia-Pacific (New Zealand, Japan, Pakistan, and the Philippines) (Ali et al., 2012a; Ali et al., 2012b; Bergh et al., 2011; Bergman et al., 2012; Dirtu et al., 2012; Dodson et al., 2012; Garcia et al., 2007; Ingerowski et al., 2001; Kanazawa et al., 2010b; Kim et al., 2013; Marklund et al., 2003; Meeker and Stapleton, 2010; van den Eede et al., 2011). Concentrations of PFRs in indoor dust have been higher than concentrations of PBDEs in recent years (Ali et al., 2012b; Dirtu et al., 2012; Dodson et al., 2012; Saito et al., 2007; Stapleton et al., 2012; van den Eede et al., 2011). In Japan, the use of PBDEs diminished in the early 1990s following the recommendation by the Japanese Flame Retardants Conference for voluntary controls (Watanabe and Sakai, 2003), and PFRs are now the most frequently used organic flame retardants in Japan (Saito et al., 2007). According to the Yearbook of Chemical Industry Statistics of Japan (2010), the production quantity and shipment quantity of phosphate plasticizers were 21,365 and 24,044 tons, respectively, in 2005, and 42,927 and 42,737 tons, respectively, in 2010. We have analyzed the levels of PFRs in floor dust samples and multi-surface dust samples in home environments in Sapporo, Japan (Kanazawa et al., 2010b), and the levels of PFRs were higher than those in other countries (Ali et al., 2012b; Bergh et al., 2011; Garcia et al., 2007; Ingerowski et al., 2001; Marklund et al., 2003; Meeker et al., 2010).

Only limited reports have been published on the human health effects of PFRs. TCEP and TDCIPP are carcinogenic in animals, and TCIPP and TBOEP are possible carcinogens (WHO 1998, 2000). TCEP has toxic effects on fetal development in mice (Chapin et al., 1997). TBOEP, TCEP, tris(2-ethylhexyl) phosphate (TEHP; 78-42-2), and TDCIPP cause mild irritation to rabbit skin (Leisewitz et al., 2000; WHO, 1991b, 1998, 2000). TNBP irritates the skin and eyes of humans (WHO, 1991a). One case report described contact dermatitis from TPHP exposure (Camarasa and Serra-Baldrich, 1992). The only epidemiological studies published regarding indoor exposure to PFRs and their health effects are from Meeker and Stapleton (2010) and Kanazawa et al. (2010a). Meeker and Stapleton (2010) reported that the level of TDCIPP in house dust shows a negative association with free thyroxin and a positive association with prolactin. In addition, the level of TPHP shows a negative association with semen quality (Meeker et al., 2010), although that particular study examined infertile men and not the general population. Previously, we showed that TNBP is associated with the occurrence of mucosal symptoms in sick building syndrome (Kanazawa et al., 2010a).

According to the latest review, which is based on data from the International Study of Asthma and Allergies in Childhood (ISAAC) survey, the prevalence of asthma among children is highest in developed countries such as Ireland and New Zealand (26.7%), the UK (27.4%), and the USA (22.3%) (Gerez et al., 2010). The prevalence of allergic rhinoconjunctivitis is also high in these countries including the USA (19.1%), New Zealand

(18.0%), Ireland (15.5%), and the UK (15.3%) (Gerez et al., 2010). Compared with these countries, the prevalence of asthma and allergic rhinoconjunctivitis is slightly lower in Japan (18.2% and 10.6%, respectively) but these percentages had increased from phase I to phase III of the study (Gerez et al., 2010). The lifetime prevalence of atopic dermatitis in Europe is highest in France (30.4%) and Sweden (26.5%), as compared with 10.6% in the UK, 8.3% in the USA, and 13.6% in Japan (Deckers et al., 2012; Gerez et al., 2010). The prevalence of atopic dermatitis also showed an increasing trend from 1996 to 2006 in Japan (Deckers et al., 2012). A nationwide cross-sectional population-based study was conducted in adults using the European Community Respiratory Health Survey questionnaire; the gender- and age-standardized prevalence of current asthma among this population is 5.3% (Fukutomi et al., 2010). As well as lifestyle changes and increased socio-economic wealth, environmental changes may also have an effect on this increased prevalence (Deckers et al., 2012). Not only biological exposure to allergens, mold, or endotoxins but also chemical pollutants in indoor air, such as phthalates and polyvinyl chloride materials, have been considered as environmental risk factors for allergies (Bornehag et al., 2005; Bornehag and Nanberg, 2010; Bornehag et al., 2004; Hsu et al., 2012; Jaakkola and Knight, 2008). Although PFRs have been analyzed in indoor dust (Ali et al., 2012a; Ali et al., 2012b; Bergh et al., 2011; Bergman et al., 2012; Dirtu et al., 2012; Dodson et al., 2012; Garcia et al., 2007; Ingerowski et al., 2001; Kanazawa et al., 2010b; Kim et al., 2013; Marklund et al., 2003; Meeker et al.,

2010; van den Eede et al., 2011), there has been no evidence regarding the association between PFRs and allergies. In this paper, we determined the levels of PFRs in house dust and investigated the relationships between PFR levels and the prevalence of asthma and allergies.

Materials and methods

The details of the study design and methods of environmental measurements have been reported previously (Araki et al., 2010; Kanazawa et al., 2010b; Kishi et al., 2009; Takigawa et al., 2010); therefore, only brief descriptions are provided here.

Study population

We studied 624 inhabitants of 182 single-family homes in six regions of Japan: Sapporo, Fukushima, Nagoya, Osaka, Okayama, and Fukuoka. This research is based on data collected between September and December, 2006. In 2003, preliminary questionnaires on indoor air quality were sent to 6,080 single-family homes based on building plan approval applications within the past 5 years in these six areas to select houses that were <7 years old; 2,297 households responded (a response rate of 41.1%) (Kishi et al., 2009). Of the responding households, 425 agreed to home visits for environmental measurements in 2004 (Saijo et al., 2011; Takigawa et al., 2010), and the first follow-up of 270 households was conducted in 2005. In 2006, the second follow-up of 182 households was conducted; these are the

households in which PFR measurements in dust had been first conducted. The original study protocol was prospective, and the inhabitants agreed to allow environmental measurements over a 3-year period. The resulting potential selection bias was analyzed by comparing the participants who continued with the study with those who did not, using the data from 2003 and 2004; no significant differences were found (Araki et al., 2010).

Outcome measures

All inhabitants of each home were asked to complete a self-administered questionnaire containing questions about age, gender, smoking status, frequency of alcohol consumption, the amount of time typically spent in the house, and self-reported stress level. Parents filled in the questionnaires for inhabitants who were <6 years old. Participants who reported having received medical treatment for bronchial asthma, atopic dermatitis, allergic rhinitis, and/or allergic conjunctivitis at any time during the preceding 2 years were classified as positive (Araki et al., 2012). Another questionnaire included questions about characteristics of the dwelling and living situations, such as the presence of environmental tobacco smoke (ETS), renovations within the preceding year, wall-to-wall carpeting, signs of dampness, hair/fur-bearing pets in the home, and the frequency of usage of mechanical-ventilation equipment. Both the personal and the housing questionnaires were distributed and collected by the investigator who visited each house at the same time as the dust sampling in 2006.

Measurement of indoor PFR levels

Dust collection, gas chromatography (GC) analytical methods, and quality assurance have been described in detail elsewhere (Kanazawa et al., 2010b; Saito et al., 2007). Briefly, dust samples were individually collected using a hand-held vacuum cleaner with a paper dust bag from all surfaces of the floor ("floor" hereafter) and from other surfaces including shelves, cupboards, frames, door frames, windowsills, TV sets, audio sets, personal computers, and interior materials such as wall and ceiling papers ("multi-surface" hereafter). To avoid cross-contamination between samples, vacuum nozzles were washed in an ultrasound bath, and vacuum cleaners were wiped with ethanol after each sample was collected. The collected dust was placed in glass tubes that had been cleaned with acetone. The tubes were sealed with polytetrafluorethylene tape and wrapped in aluminum foil and were stored and transported at −20°C until analysis. Contaminants such as pieces of food, hair, feathers, and insects were removed from dust samples with tweezers, and then 1 ml acetone per 25 mg dust was added to each dust sample (25−50 mg dust/sample). Samples were ultrasonicated for 20 min and allowed to stand overnight. An internal standard (IS), 0.1 μg/ml tris(*1H,1H,5H*-octafluoropentyl)phosphate, was added to each sample for monitoring and quantification. After centrifugation at 2500 × *g* for 10 min, the supernatants were injected onto a DB-17 column (J&W Scientific Inc., Lolsom, CA, USA) for GC/flame photometric

detection (GC-FPD; using an Agilent 6890 GC-FPD, Agilent Technologies Inc., Palo Alto, CA, USA) at the Tokyo Metropolitan Institute of Public Health in Tokyo, Japan. The operating conditions for GC-FPD are shown in Table S1.

Quality assurance and quality control

Calibration curve was constructed using six different concentrations (0.05, 0.1, 0.5, 1.0, 2.0 or 5.0 μg/ml for each of the eleven compounds) together with IS (0.1 μg/ml) in acetone for GC-FED analysis. Good linear correlations between the concentration of target compounds and the ratio of the peak area of each compound with respect to the IS were obtained. Recovery rates were examined using dust samples. After 50 ng of each PFR (except for TMPP, for which 500 ng was added) was individually added to 50-mg dust samples, the air-dried samples were extracted with 1 ml acetone and analyzed by GC-FPD (n = 3). Recovery rates ± standard deviations ranged from 96.3 ± 7.2% for TPHP to 82.7 ± 9.7% for TCIPP (Table S2). Since the observed levels of TBOEP in indoor dust samples were remarkably higher than other compounds, recovery rate of spiking 2 μg of TBOEP was also examined. As a result, recovery rate ± standard deviation was 95.0 ± 2.6 %. The instrumental limit of detection (LOD) was defined as the absolute amount of an analyte that yielded a signal-to-noise ratio of 3 (Table S2). Gas chromatograms of PFRs in the standard solution, an acetone blank, and an indoor floor dust sample are shown in Figure S1. The method detection limits (MDLs) were

calculated based on the LODs, the sample weight, and the volume of the extract. The calculated MDL for each PFR in a 25-mg sample of dust is shown in Table 1; if the concentrations were below the MDL, they were assigned a value of half the MDL. A PFR was identified when its peak was within ±5 seconds of the retention time of a specific PFR in the calibration standard and the relative noise intensity was within ±20% of that from the standard PFR. Quantification of each PFR was first determined based on the peak area ratio of the standard curve, and then the concentrations of individual PFRs in the dust samples (Cd) (μg/g) were calculated based on Equation 1:

$$\mathrm{Cd} = [(As - At) \times E] \div (v \times W) \qquad (1)$$

where *As* is the sample weight injected for GC-FPD (ng), *At* is the weight of the travel blank injected for GC-FPD (ng), *E* is the extract volume (ml), *v* is the injected volume (μl), and *W* is the weight (g) of the dust sample that was used for extraction. To avoid PFR contamination, all glass tubes and stainless steel equipment for sample collection and analysis were ultrasonicated for 10 min in acetone, rinsed with acetone, and then air dried. To examine the background levels of PFRs from materials used for sampling, the vacuum dust bag and the ethanol-soaked cotton used to wipe the vacuum nozzle were extracted with acetone and analyzed by GC-FPD to confirm that there were no PFR peaks (data not shown). Thus, the background level of PFRs was negligible, as described previously (Kanazawa et al., 2010b; Saito et al., 2007).

Measurement of environmental dust mite allergens, airborne fungi, formaldehyde, and volatile organic compounds (VOCs)

Mite allergen levels of *Dermatophagoides pteronyssinus* allergens (Der p1) and *Dermatophagoides farinae* allergens (Der f1) in floor dust were determined with enzyme-linked immunosorbent assays (Ogino et al., 2002; Saijo et al., 2011). When allergen levels were less than the LOD of 0.1 μg/g of fine dust, they were given a value of 0.05 μg/g. The sum of the values for Der p1 and Der f1 were combined into a single factor, called Der1.

The method for identifying individual genera of fungi and for counting the total number of colonies (colony-forming units or CFU/m^3) has been described by Takahashi (1997) and Saijo et al. (2011). For the transformation of data to logarithmic values, samples with no colonies were given a value of 0.5 CFU/m^3 (Saijo et al. 2011).

Formaldehyde and VOC measurements were conducted using the method described by Takigawa et al. (2010) and Araki et al. (2009), respectively. Briefly, for the detection of formaldehyde, samples were collected with the passive sampler Supelco DSD-DNPH (Sigma-Aldrich, Lt. Louis, MO, USA) and analyzed with high-performance liquid chromatography. To detect VOCs, samples were collected using the passive sampler Supelco VOC-SD (Sigma-Aldrich, Lt. Louis, MO, USA) and analyzed with GC/mass spectrometry at the Japan Industrial Safety and Health Association in Tokyo, Japan. When formaldehyde and

VOC concentrations were lower than their respective LODs, they were given a value of half the LOD. The sum of the 29 VOCs analyzed was treated as a single factor (Araki et al., 2010).

Data analysis

Of the 182 houses, 156 were included in the analysis as contributing either a floor or multi-surface dust sample that was >25 mg. For floor dust and multi-surface dust, 148 and 120 houses, respectively, yielded samples that were >25 mg. Dust samples of >25 mg were collected from both the floors and multi-surfaces from 112 houses, and these samples were used to analyze the relationship between floor and multi-surface dust. Levels of PFRs in floor dust and multi-surface dust were compared using the Wilcoxon matched rank test. In some cases, the sum of the eleven PFRs examined here (ΣPFRs) was analyzed. Correlation coefficient values between floor dust and multi-surface dust and between individual PFRs were calculated with Spearman's rank correlation test. Housing characteristics were analyzed with the Mann-Whitney U-test. The relationships between characteristics of the inhabitants and housing characteristics and disease prevalence were calculated with the χ^2 test. To determine the relationships between the prevalence of disease and the concentrations of PFRs, statistical analysis was conducted using logistic regression, and the odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. The PFR data was not normally distributed based on the Kolmogorov-Smirnov test, so that each PFR concentration was

$\log_{10}$-transformed before analysis. Although some PFRs were still not normally distributed, distributions became near to normal after the data were transformed. First, crude ORs and 95% CIs were calculated. Then, asthma and allergic symptoms were adjusted for gender, age group (divided into 15-year blocks), tobacco smoking, ETS exposure, and housing characteristics that were significantly or marginally ($p < 0.1$) related to one or more medical outcomes. The dampness index (0–5) was calculated by summing the number of signs of dampness observed in each dwelling based on the five signs described by Kishi et al. (2009) and Saijo et al. (2011). When the p-value in the crude model was <0.1, other environmental variables were also included in the adjusted models. The effect of each PFR was modeled separately. SPSS for Windows version 14.0J (SPSS Inc., Chicago, IL, USA) was used for the analysis; a 5% significance level was applied.

Ethical considerations

The study protocol was approved by the ethics board for epidemiological studies at the Hokkaido University Graduate School of Medicine and by the ethics boards at all of the regional universities involved in the study. All participants and their parents, when relevant, gave written informed consent to participate in the study.

Results

Table 1 shows the distribution of PFRs and other environmental measurements. The most frequently detected and the most concentrated PFR was TBOEP for both floor and multi-surface dust, followed by TCIPP. For trimethyl phosphate (TMP, 512-56-1), triethyl phosphate (TEP, 78-40-0), tripropyl phosphate (TPP, 513-08-6), and TMPP, fewer than 11% of samples had detection levels higher than the MDL for both floor and multi-surface dust, and no further analysis was conducted for these compounds. There were positive correlations for PFR levels between floor dust and multi-surface dust from $\rho = 0.205$ to 0.697 ($p < 0.01$). The levels of TEHP and TBOEP were significantly higher in floor dust than multi-surface dust, whereas levels of TCIPP, TDCIPP, and TPHP were significantly higher in multi-surface dust than floor dust. To find the effect of mixtures of PFRs, ΣPFRs was analyzed as well as the individual PFRs**.** A plot of ΣPFRs from floor dust and multi-surface dust is shown in Figure S2. Total VOCs may be an indicator of the indoor air chemical environment and may be related to airway symptoms (Wieslander et al., 1997). Thus total VOC concentrations were used as possible confounders of indoor chemical factors (Saijo et al., 2011). Correlations between individual PFRs are shown in Table 2. There were weak but significantly positive correlations between most PFR levels. Associations between housing characteristics and PFR levels are shown in Table 3. Significantly higher levels of TBOEP were obtained for wood floors than for other types of flooring, such as carpeting, tile, stone, or *tatami*.

Wooden-structure houses showed higher levels of multi-surface TCIPP, TCEP, and TPHP than other types of houses, such as reinforced concrete houses. Houses using mechanical ventilation often showed higher levels of PFRs than houses that rarely used mechanical ventilation or those without an installed mechanical ventilation system.

Of the 624 inhabitants, outcomes and exposure measurements could not be obtained for 108 individuals, and thus the results reflect data for 516 inhabitants from 156 different homes. Table 4 summarizes the demographic data, smoking status, and prevalence of allergy treatment. The prevalence of asthma, atopic dermatitis, allergic rhinitis, and allergic conjunctivitis in the preceding 2 years was 4.7%, 10.3%, 18.6%, and 7.6%, respectively, among these individuals.

Table 5 shows the relationships among asthma, allergies, and the participants' personal and housing characteristics. Asthma and allergies were more prevalent in the younger age groups. The following housing characteristics were significantly or marginally ($p < 0.1$) related to one or more medical outcomes: housing renovation within the preceding year, wall-to-wall carpeting, dampness index, hair/fur-bearing pets in the dwelling, and mechanical ventilation use.

Relationships between levels of PFRs and asthma and allergies are shown in Table 6 (adjusted statistics). Unadjusted statistics are shown in Table S3. After adjustment for gender, age, tobacco smoke, ETS exposure, recent renovations, wall-to wall carpeting,

dampness index, hair/fur-bearing pets in the dwelling, mechanical-ventilation equipment usage, and total fungi, positive relationships were found between asthma and TNBP in floor and multi-surface dust, between atopic dermatitis and TCIPP and TDCIPP in floor dust, and between allergic rhinitis and TNBP in multi-surface dust.

Discussion

In this study, to ensure the validity of the analysis of PFRs, only dust samples that exceeded 25 mg were included in the analysis. All asthma and allergy-related health effects examined here were more prevalent in the younger age groups, but there were no differences between males and females. The following housing characteristics were significantly or marginally related to medical outcomes: housing renovation within the preceding year, wall-to-wall carpeting, and dampness index. The distribution of formaldehyde, total VOCs, fungi, and the Der1 concentration in Table 1 were not different from the values we previously reported for all 182 houses (Araki et al., 2012). Demographic data for the participants, the prevalence of asthma and allergies, and the relationships between these illnesses and personal and housing characteristics in Tables 4 and 5 showed the same trend as in a previous report that included all 609 inhabitants (Araki et al., 2012). Therefore, there was minimal potential selection bias that was attributable to the weight of the collected dust samples.

Levels of PFRs and comparison with other studies

Contaminant levels of PFRs in indoor dust have been reported for several countries (Ali et al., 2012a; Ali et al., 2012b; Bergh et al., 2011; Bergman et al., 2012; Dirtu et al., 2012; Dodson et al., 2012; Garcia et al., 2007; Ingerowski et al., 2001; Kanazawa et al., 2010b; Kim et al., 2013; Marklund et al., 2003; Meeker et al., 2010; van den Eede et al., 2011). In Europe, the dominant compounds in indoor dust are TBOEP, TCIPP, TCEP, TPHP, and TDCIPP, with median values reaching up to 9.9 μg/g for TBOEP (Bergh et al., 2011; Dirtu et al., 2012; Garcia et al., 2007; Marklund et al., 2003; van den Eede et al., 2011). Similar to the findings from Spain, the compounds that were detected most in our present study were TBOEP, followed by TCIPP, TCEP, TPHP, and TDCIPP. In the USA, two compounds, TDCIPP and TPHP, have been measured, with median values of 5.47 μg/g and 1.75 μg/g, respectively (Meeker et al., 2010). The levels of TDCIPP and TPHP in our study were similar to levels in the USA and were higher than those in Europe, New Zealand, Pakistan, and the Philippines (Ali et al., 2012a; Ali et al., 2012b; Bergh et al., 2011; Dirtu et al., 2012; Garcia et al., 2007; Kim et al., 2013; Marklund et al., 2003; Meeker et al., 2010; van den Eede et al., 2011). In Pakistan, TBOEP, TNBP, and TPHP were measured, and their median values were up to 0.094 μg/g (Ali et al., 2012b). It is of note that for TBOEP the median value in floor dust was 508 μg/g in our study, which was 200- to 10,000-fold higher than the value measured at home in

any other country. A similar median level of TBOEP was reported in a daycare in Sweden (Bergh et al., 2011). TBOEP is often used in floor polish agents and as a plasticizer in vinyl plastics (Marklund et al., 2003; WHO 2000). In our study, 92.3% of the houses had wooden floors, and 64.8% had polyvinyl chloride wall coverings. Significantly higher levels of TBOEP were obtained from wooden floors than for other types of flooring, such as carpeting, tile, stone, or *tatami* (median value of 544.3 μg/g and 93.1 μg/g, respectively; Mann-Whitney U-test, $p = 0.016$). Kanazawa et al. (2010a) reported PFR levels in Sapporo, Japan, and the present study includes the levels of PFR from five cities in Japan as well as from Sapporo. Dwellings in Sapporo contain remarkably high levels of TBOEP in floor dust (Kanazawa et al., 2010a). One reason for this result could be that Sapporo is located in northern Japan, and thus houses in Sapporo tend to be more air-tight and have thicker insulation than do houses in other areas of the country (Kanazawa et al., 2010a). Another possible reason is that the percentage of homes with wooden floors is higher in Sapporo (97.5%) than in six areas (83.6%) (Table 3).

Levels of PFRs and housing characteristics

TCIPP and TCEP are used in flexible and rigid polyurethane foams (Stapleton et al., 2009) and are used for sealing and heat-insulating materials. However, we did not evaluate insulation in this study, and the association between TCIPP and insulation for this study

population is unknown. Levels of some PFRs were significantly higher in houses that use mechanical ventilation than in those that do not. Emission rates of PFRs may increase when the concentration in the air decreases, probably because the concentration in a material tends to remain at near-equilibrium with the concentration in the air (Afshari et al., 2004). Another possibility, which seems to be a more convincing hypothesis, is that mechanical-ventilation equipment usage may be related to the frequency of window opening. Levels of some PFRs were significantly higher in houses for less frequently open windows than in those for more frequently open windows (Table 3). Inhabitants who open windows for a less frequently were more likely to use mechanical ventilation equipment (χ^2 test; $p = 0.010$) (data not shown). Therefore, lower levels of PFRs in houses that do not use mechanical ventilation than in houses that do use ventilation may be confounded by the effects of window opening. Bergh et al. (2011) compared the level of PFRs in the air between buildings at a high risk of sick building syndrome (SBS) and those at a low risk and found no difference in the concentrations of PFRs. In addition, greater differences in PFR levels within buildings than between buildings indicate that it is important to focus on the materials introduced into individual residences by the inhabitants in future studies (Bergh et al., 2011).

Comparison between multi-surface dust and floor dust

The levels of PFRs tended to be higher in multi-surface dust than in floor dust. Similarly,

Bjorklund et al. (2012) measured PBDE levels and found that the concentrations of individual PBDE congeners were higher in above floor–settled dust than in floor dust. In our present study, the method of dust collection was the same for multi-surface and floor dust. The participants in this study reported floor vacuuming every 2 days on average, but the frequency with which they reported cleaning furniture and windowsills at the same time was 39.6% and 23.1%, respectively (data not shown). Therefore, multi-surface dust reflects conditions over longer periods than does floor dust. However, Bjorklund et al. (2012) concluded that the explanation that older dust accumulates higher brominated flame retardant concentrations is less likely because PBDEs should reach equilibrium within hours to days. The air partition coefficient for octanol is smaller than that for PBDEs (Weschler and Nazaroff, 2008), suggesting that the hypothesis that older multi-surface dust accumulates higher PFR concentrations is less likely as well. Multi-surface dust was in direct contact with TV sets, other electronics, and furniture, which are the main emitting sources of PFRs (Saito et al., 2007; Stapleton et al., 2009). Thus, higher concentrations of PFRs in multi-surface dust than in floor dust are expected.

Asthma, allergies, and levels of PFRs

The present study found that the level of TNBP was related to the inhabitant's medical treatment for asthma and allergic rhinitis. Kanazawa et al. (2010a) showed a significant and

strong association between TNBP in floor dust and house-related mucous symptoms among individuals. The levels of TCIPP and TDCIPP were related to the inhabitant's recent medical treatment for atopic dermatitis. We analyzed the sum of the eleven PFRs (ΣPFRs) and calculated an odds ratio (OR) for each of the health outcomes. Because TBOEP is the predominant PFR in these samples, the ORs for ΣPFRs were similar to those for TBOEP, which were not significantly associated with any of these health outcomes. Measurements of dust mite allergens, airborne viable fungi, and the concentration of formaldehyde, VOCs in the air were performed at the same time in the present study. Airborne fungi are related to atopic dermatitis (Table S3), and this variable was included in the adjusted model. Dust mite allergens are known environmental risk factors for allergies (Arshad, 2005), but are not related to allergies in this study. 1-Octen-3-ol, one of the known MVOCs related to allergic rhinitis and allergic conjunctivitis in the same study (Araki et al., 2012). Since we could not introduce too many predictive variables into the model due to the small sample size and low prevalence of allergies, Der1 and 1-octen-3-ol were not included in the models shown in Table 6. However, when we examined data for our current model in conjunction with Der1 and 1-octen-3-ol, the associations between allergies and PFRs showed similar trend. The conclusions in this paper are not in contradiction with our previous paper.

TCIPP, TEHP, and TDCIPP are classified as mild-to-moderate irritants of rabbit skin, and slight erythema is observed after rabbit skin is exposed to these compounds for 1 day

(WHO, 1998, 2000). In addition, TCIPP and TDCIPP are irritating to the skin and eyes of rats (Leisewitz et al., 2000; van der Veen et al., 2012). A case report of allergic contact dermatitis from TPHP has been reported (Camarasa et al., 1992). According to a WHO report (1991a), TNBP is slightly irritating to rabbit eyes, suggesting that this compound adversely affects mucosal membranes. Interestingly, associations between TCIPP and TDCIPP and dermatitis were obtained only from floor dust, although the levels of these PFRs were lower in the floor dust than in the multi-surface dust. The dust in this study was collected in the living room. In Japan, inhabitants generally take off their shoes in the house and sit on the floor when relaxing. Therefore, the inhabitants may have had higher skin contact and exposure to floor dust than to multi-surface dust, possibly explaining why stronger associations between symptoms and floor dust were obtained.

This study has several limitations. First, this was a cross-sectional study, and any causal relationships between exposure and outcomes could not be determined. It should also be noted that because of the number of PFRs and associations that were examined, statistically significant relations between the levels of PFRs and outcomes could be obtained by chance. Second, various factors influence the prevalence of allergic diseases, and we could not take all factors into account. Some known environmental factors that affect allergies in the home, such as dust mite allergens and mold, were considered. However, other factors such as

particle matters were not considered. Indoor settled dust contains many different chemicals such as PBDE, perfluorinated compounds, pesticides, and phthalates (Bonvallot et al., 2010). It is difficult to exclude a contribution by other chemicals in dust, and the presence of other chemicals in the dust may have affected our results. Third, the environmental measurements were conducted only once. In addition, the samples were collected from only one room in each house. The location and season for sampling may substantially influence the level of contamination detected (Muenhor and Harrad, 2012). All dust samples were collected from the main living area of each house. Most residents seem to stay in the main living area for many hours, except when they are sleeping; therefore, we considered the exposure levels of inhabitants in their living rooms to represent the overall exposure levels in the dwellings (Saijo et al., 2011). Fourth, we did not sieve the dust samples analyzed here. Dust with a particle size of <100 μm may be of greater concern, and fine particles adhere better to human's hands or skin than larger particles (Cao et al., 2012). The use of sieved samples in the future may uncover additional or stronger associations. Fifth, environmental measurements were made only in participants' homes, and potential exposure in areas outside of their homes, such as in offices or schools, was not considered. Finally, outcome measures in this study were obtained using questionnaires, and immunoglobulin E and other allergy markers were not measured. Asthma and allergy were considered to be positive when the participant reported taking asthma or allergy medications within the preceding 2 years. Therefore,

misclassification of the medical outcomes could have occurred. In addition, the severity of the conditions and the frequency of medical treatment were not considered. The participants had lived in the same house for more than 2 years, and thus chronic exposure from their homes may have remained within a similar range over the preceding years. We consider this to be a strength of this study.

Conclusions

The levels of PFRs in Japan were higher when compared with those from studies performed in Europe, the USA, and Pakistan. The level of TBOEP in particular was much higher than that in any other country except the daycare results from Sweden. The results show positive correlations between the levels of TCIPP and TDCIPP and atopic dermatitis, as well as between TNBP and asthma and rhinitis. Although this is a preliminary finding, evaluating health risks associated with chronic indoor exposure to PFRs may have important public health implications. Thus, further studies are needed to confirm these results.

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Table 1 Distribution of PFRs and other environmental variables

	Floor (n = 148)							Multi-surface (n = 120)							
	MDL	＞MDL (%)	Minimum	25th	Median	75th	Maximum	＞MDL (%)	Minimum	25th	Median	75th	Maximum	ρ [e]	p[f]
PFR[a]															
TMP	1.02	0.0					<MDL	0.0					<MDL	ND	ND
TEP	0.52	9.8				<MDL	2.80	7.5				<MDL	3.31	ND	ND
TPP	0.49	0.7				<MDL	1.13	0.0					<MDL	ND	ND
TNBP	0.73	63.0		<MDL	1.03	1.84	132.75	73.3		<MDL	1.15	1.79	42.76	0.355**	0.982
TCIPP	1.12	97.3	<MDL	3.83	8.69	22.25	429.50	100.0	1.3	10.39	25.81	59.69	462.37	0.550**	<0.001
TCEP	1.30	93.9	<MDL	2.98	5.83	11.61	338.45	90.8	<MDL	4.12	8.26	17.37	2,320.00	0.448**	0.054
TEHP	1.34	64.2		<MDL	2.07	4.49	51.02	56.7		<MDL	1.47	2.50	73.06	0.351**	<0.001
TBOEP	1.20	100.0	6.24	137.65	508.32	1417.50	5,890.00	100.0	5.29	48.36	110.51	271.97	14,100.00	0.697**	<0.001
TDCIPP	1.18	67.6		<MDL	2.80	11.18	864.04	95.0	<MDL	4.51	10.81	24.14	593.14	0.205**	<0.001
TPHP	1.60	88.5	<MDL	2.81	4.51	7.64	245.08	94.2	<MDL	6.12	11.54	28.79	889.18	0.207**	<0.001
TMPP	4.00	6.1				<MDL	59.83	10.8				<MDL	193.1	ND	ND
∑PFRs	ND	ND	33.94	197.30	576.73	1,461.44	5,979.85	ND	17.35	150.67	243.74	440.35	15,087.35	0.629**	<0.001

Other environmental variables (n = 156)

	LOD	＞LOD (%)	Minimum	25th	Median	75th	Maximum
Formaldehyde[b]	5	99.5	<LOD	22.3	32.6	47.8	120.1
Total VOCs[b]	10	85.2	<LOD	16.0	48.5	86.1	2,798.9
Total fungi[c]	0	98.9	0	120	310	597.5	3,490
Der1[d]	0.10	94.2	<LOD	0.70	2.76	9.90	502.3

LOD. limit of detection; MDL, method detection limit(<MDL indicates that a concentration equal to half of the calculated MDL for that PFR was used in the calculations); ND, not determined; PFRs, organophosphate esters; TBOEP, tris(2-butoxyethyl) phosphate; TNBP, tributyl phosphate; TCEP, tris(2-chloroethyl) phosphate; TCIPP, tris(2-chloro-*iso*-propyl) phosphate; TMPP, tricresyl phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TEP, triethyl phosphate; TMP, trimethyl phosphate; TPHP, triphenyl phosphate; TPP, tripropyl phosphate; VOCs, volatile organic compounds

Units: [a]μg/g dust; [b]μg/m^3; [c]colony forming unit (CFU)/m^3; [d]μg/g fine dust

[e]Correlation coefficient values were calculated with Spearman's rank correlation test (n = 112); **p < 0.01

[f]Significant differences between floor and multi-surface dust were assessed with the Wilcoxon matched rank test (n = 112)

Table 2 Correlations between individual PFRs

PFR	TBP	TCIPP	TCEP	TEHP	TBOEP	TDCIPP	TPHP
Floor							
TBP	1	0.290**	0.494**	0.293**	0.076	0.154	0.200*
TCIPP		1	0.495**	0.447**	0.278**	0.273**	0.319**
TCEP			1	0.450**	0.285**	0.272**	0.451**
TEHP				1	0.733**	0.104	0.259**
TBOEP					1	–0.032	0.209*
TDCIPP						1	0.186*
TPHP							1
Multi-surface							
TBP	1	0.282**	0.426**	0.136	0.145	0.089	0.373**
TCIPP		1	0.148	0.289**	0.144	0.516**	0.350**
TCEP			1	0.154	0.163	0.190*	0.391**
TEHP				1	0.413**	0.268**	0.312**
TBOEP					1	0.385**	0.222*
TDCIPP						1	0.398**
TPHP							1

PFRs, organophosphate esters; TBOEP, tris(2-butoxyethyl) phosphate; TNBP, tributyl phosphate; TCEP, tris(2-chloroethyl) phosphate; TCIPP, tris(2-chloro-*iso*-propyl) phosphate; TMPP, tricresyl phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TEP, triethyl phosphate; TMP, trimethyl phosphate; TPHP, triphenyl phosphate; TPP, tripropyl phosphate

Correlation coefficient values were calculated with Spearman's rank correlation test; *$p < 0.05$, **$p < 0.01$

Table 3 Relationships between housing characteristics and levels of PFRs

			TBP		TCIPP		TCEP		TEHP		TBOEP		TDCIPP		TPHP	
		n	median	p	median	p	median	p	median	p	median	p	median	p	median	p
Floor																
Structural material	Wooden	120	.99	0.918	10.90	0.251	5.34	0.483	2.14	0.895	504.0	0.929	2.58	0.469	4.16	0.896
	Other	25	.99		6.06		4.88		1.84		577.0		4.09		4.07	
Age of house	3-5 years	101	1.13	0.881	22.40	0.133	7.14	0.605	1.63	0.862	116.0	0.693	10.80	0.668	11.10	0.280
	6-8 years	23	.99		10.90		5.34		2.14		504.0		2.58		4.16	
Renovation within the preceding year	Yes	7	1.41	0.113	8.13	0.629	4.77	0.942	4.51	0.244	616.0	0.714	3.22	0.858	5.06	0.790
	No	141	1.02		9.11		5.91		2.02		504.0		2.75		4.50	
Wall materials	PVC	120	1.02	0.550	9.11	0.703	5.91	0.826	2.02	0.206	504.0	0.125	2.75	0.068	4.50	0.334
	Other	28	1.05		7.87		4.50		1.25		306.0		5.03		4.01	
Floor material	Wooden	135	1.02	0.622	8.17	0.692	5.91	0.660	2.14	0.297	**544.0**	**0.002**	2.58	0.314	4.55	0.652
	Other	13	1.21		9.36		5.28		1.82		**93.1**		3.77		4.16	
Wall-to-wall carpeting	Yes	6	1.61	0.085	3.68	0.613	4.03	0.853	1.20	0.155	223.0	0.093	2.74	0.703	5.43	0.730
	No	142	1.02		8.98		5.95		2.11		515.0		2.86		4.51	
frequency of window opening	>15 times/month	110	1.02	0.348	**7.51**	**0.009**	**4.98**	**0.034**	**1.82**	**0.006**	**404.4**	**0.013**	2.66	0.722	4.22	0.107
	≦14times/month	33	1.18		**17.58**		**7.04**		**4.17**		**1,009.9**		3.25		5.40	
Mechanical-ventilation equipment usage	Always/often/occasionally	56	1.07	0.375	12.70	0.067	6.91	0.058	**2.98**	**0.013**	**515.0**	**0.043**	3.98	0.124	5.17	0.433
	Never/no ventilation	89	1.02		6.75		4.70		**1.75**		**402.0**		2.42		4.23	
Multi-surface																
Structural material	Wooden	98	1.10	0.676	**30.10**	**0.013**	**9.22**	**0.033**	1.53	0.220	111.0	0.631	12.50	0.079	**11.80**	**0.040**
	Other	19	1.32		**11.40**		**5.53**		0.67		93.7		9.15		**6.86**	
Age of house	3-5 years	87	1.06	0.615	**22.40**	**0.049**	7.38	0.589	1.49	0.873	111.0	0.809	10.70	0.266	11.20	0.485
	6-8 years	17	1.10		**56.90**		7.77		0.67		79.9		18.90		12.30	
Renovation within the preceding year	Yes	7	1.28	0.773	22.30	0.836	6.66	0.618	0.67	0.912	62.9	0.951	8.10	0.538	8.91	0.260
	No	113	1.13		26.28		8.77		1.49		110.0		10.90		11.90	
Wall materials	PVC	99	1.18	0.848	26.30	0.904	9.16	0.325	1.44	0.456	111.0	0.931	12.20	0.604	11.90	0.150
	Other	21	1.06		24.20		6.20		1.65		107.0		7.91		9.10	
Floor material	Wooden	109	1.18	0.707	25.30	0.845	8.00	0.390	1.57	0.119	**112.0**	**0.016**	10.80	0.975	12.30	0.205
	Other	11	1.05		26.30		8.52		0.67		**36.5**		12.30		7.89	
Wall-to-wall carpeting	Yes	4	1.17	0.859	16.90	0.342	7.31	0.650	1.84	0.206	131.0	0.826	14.40	0.884	21.60	0.396
	No	116	1.15		26.70		8.26		1.43		109.0		10.70		11.40	
Frequency of window opening	>15 times/month	86	1.20	0.518	**22.46**	**0.034**	7.33	0.197	**1.01**	**0.002**	108.9	0.591	**10.31**	**0.046**	**10.94**	**0.023**
	≦14times/month		1.18		**36.69**		12.05		**2.43**		149.6		**15.88**		**21.61**	
Mechanical-ventilation equipment usage	Always/often/occasionally	47	1.10	0.878	**36.60**	**0.029**	11.30	0.234	**1.92**	**0.019**	150.0	0.077	**17.10**	**0.001**	14.50	0.282
	Never/no ventilation	72	1.25		**18.80**		7.33		**0.67**		93.1		**7.93**		11.30	

PFRs, organophosphate esters; PVC, poly vinyl chloride; TBOEP, tris(2-butoxyethyl) phosphate; TNBP, tributyl phosphate; TCEP, tris(2-chloroethyl) phosphate; TCIPP, tris(2-chloro-*iso*-propyl) phosphate; TMPP, tricresyl phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TPHP, triphenyl phosphate;
Unit: µg/g dust
The p-values were calculated using the Mann-Whitney U-test

Table 4 Characteristics of and prevalence of allergies and symptoms among 516 inhabitants of homes that were analyzed for PFRs

	Total		Male		Female	
Characteristic	n	(%)	n	(%)	n	(%)
Gender						
Male	251	48.6				
Female	265	51.4				
Age (years)						
0–14	126	24.4	64	25.5	62	23.4
15–29	63	12.2	34	13.5	29	10.9
30–44	139	26.9	59	23.5	80	30.2
45–59	105	20.3	52	20.7	53	20.0
60+	83	16.1	42	16.7	41	15.5
Tobacco smoking						
Current smoker	49	9.5	39	15.5	10	3.8
Non-smoker, ETS at home	74	14.3	25	10.0	49	18.5
Non-smoker, no ETS at home	393	76.2	187	74.5	206	77.7
Allergic prevalence						
Asthma	24	4.7	14	5.6	10	3.8
Atopic dermatitis	53	10.3	29	11.6	24	9.1
Allergic rhinitis	96	18.6	41	16.3	55	20.8
Allergic conjunctivitis	39	7.6	18	7.2	21	7.9

ETS, environmental tobacco smoke

No significant differences were seen among any of these characteristics.

Table 5 Relationships between asthma and allergies and personal and living-space characteristics among 516 inhabitants of homes that were analyzed for PFRs

Predictors	**Subgroup**	n	Asthma (%)	*P*	Atopic Dermatitis (%)	*P*	Allergic Rhinitis (%)	*P*	Allergic conjunctivitis (%)	*P*
Personal characteristics										
Gender	Male	251	5.6	0.405	11.6	0.386	16.3	0.214	7.2	0.868
	Female	265	3.5		9.1		20.8		7.9	
Age group (years)	0–14	126	**11.9**	**<0.001**	**22.2**	**<0.001**	**31.0**	**<0.001**	**14.3**	**0.007**
	15–29	63	**4.8**		**19.0**		**20.6**		**9.5**	
	30–44	139	**2.2**		**5.0**		**16.5**		**6.5**	
	45–59	105	**1.9**		**3.8**		**14.3**		**3.8**	
	60+	83	**1.2**		**2.0**		**7.2**		**2.4**	
Smoking status	Smoker	49	0.0	0.148	**0.0**	**0.027**	14.3	0.058	2.0	0.273
	Non-smoker, ETS	74	2.7		**8.1**		28.4		6.8	
	Non-smoker, no-ETS	393	5.6		**12.0**		17.3		8.4	
Frequency of alcohol consumption	≥Once/week	179	1.7	0.081	6.1	0.174	15.1	0.175	3.4	0.004
	<Once/week	284	5.3		9.9		20.4		10.6	
Time spent in the home	17 h +	178	5.1	0.658	8.4	0.442	19.7	0.722	5.6	0.293
	<17 h	335	4.2		11.0		18.2		8.7	
Housing characteristics										
Structural material	Wooden	420	4.3	0.409	10.2	0.850	19.5	0.298	7.1	0.384
	Other	91	6.6		11.0		14.3		9.9	
Age of house	3–5 years	435	4.4	0.390	9.9	0.422	19.1	0.528	8.3	0.245
	6–8 years	78	6.4		12.8		15.4		3.8	
Renovation within the preceding year	Yes	23	**21.7**	**<0.001**	21.7	0.076	30.4	0.166	**21.7**	**0.023**
	No	493	**3.9**		9.7		18.1		**6.9**	
Wall-to-wall carpeting	Yes	19	5.3	0.602	21.1	0.120	26.3	0.371	**21.1**	**0.047**
	No	497	4.6		9.9		18.3		**7.0**	
Visible mold growth	Yes	414	4.6	0.798	10.4	1.000	20.0	0.117	**8.9**	**0.012**
	No	102	4.9		9.8		12.7		**2.0**	
Condensation	Yes	536	5.6	0.173	10.4	1.000	20.5	0.141	8.4	0.367
	No	158	2.5		10.1		14.6		5.7	
Moldy odor	Yes	105	6.7	0.300	10.2	1.000	21.0	0.575	11.4	0.094
	No	407	4.2		10.3		18.2		6.4	
High air humidity in the bathroom	Yes	101	4.0	1.000	6.9	0.274	20.8	0.570	7.9	0.836
	No	412	4.9		11.2		18.2		7.5	
Water leakage within preceding 5 years	Yes	46	8.7	0.258	13.0	0.455	13.0	0.426	0.0	0.038
	No	468	4.3		10.0		19.0		8.3	
Hair/fur-bearing pets in the dwelling	Yes	145	2.8	0.249	6.2	0.054	21.4	0.379	8.3	0.715
	No	366	5.2		12.0		17.8		7.4	
Frequency of window opening	>15 times/month	394	5.8	0.063	9.9	0.581	19.0	0.774	7.9	1.000
	≦14times/month	100	1.0		12.0		17.0		7.0	
Mechanical-ventilation equipment usage	Always/often/occasionally	194	4.1	0.671	13.9	0.050	21.6	0.242	9.3	0.310
	Never/no ventilation	309	5.2		8.1		17.2		6.8	

ETS, environmental tobacco smoke

The p-values were calculated using χ^2 tests

Table 6 Adjusted models of relationships between asthma and allergies and PFRs

	Asthma		Atopic dermatitis		Allergic rhinitis		Allergic conjunctivitis	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Floor								
TNBP	**2.85 (1.23–6.59)**	**0.014**	1.56 (0.83–2.95)	0.163	0.77 (0.45–1.34)	0.355	0.88 (0.40–1.94)	0.751
TCIPP	0.87 (0.33–2.35)	0.794	**2.43 (1.28–4.61)**	**0.006**	0.99 (0.62–1.58)	0.972	0.78 (0.38–1.64)	0.517
TCEP	1.16 (0.42–3.28)	0.778	1.66 (0.82–3.35)	0.159	1.22 (0.74–2.00)	0.437	1.01 (0.47–2.19)	0.975
TEHP	2.16 (0.73–6.42)	0.163	1.83 (0.82–4.07)	0.142	1.59 (0.87–2.90)	0.132	0.51 (0.19–1.38)	0.187
TBOEP	1.15 (0.51–2.62)	0.733	1.01 (0.57–1.81)	0.963	1.27 (0.83–1.93)	0.276	0.88 (0.47–1.65)	0.688
TDCIPP	1.85 (0.96–3.58)	0.067	**1.84 (1.17–2.88)**	**0.008**	0.82 (0.57–1.18)	0.282	1.45 (0.86–2.45)	0.168
TPHP	1.60 (0.55–4.67)	0.389	1.86 (0.92–3.75)	0.083	1.12 (0.63–1.99)	0.699	1.27 (0.52–3.07)	0.604
∑PFRs	1.32 (0.51–3.45)	0.572	1.28 (0.64–2.54)	0.485	1.31 (0.80–2.15)	0.277	0.82 (0.39–1.72)	0.603
Multi-surface								
TNBP	**5.34 (1.45–19.7)**	**0.012**	1.27 (0.49–3.30)	0.629	**2.55 (1.29–45.01)**	**0.007**	1.68 (0.59–4.77)	0.334
TCIPP	1.26 (0.55–2.87)	0.588	0.92 (0.44–1.95)	0.835	1.43 (0.82–2.53)	0208	1.15 (0.46–2.87)	0.772
TCEP	1.58 (0.36–6.92)	0.544	1.02 (0.56–1.86)	0.944	1.27 (0.83–1.95)	0.272	1.20 (0.61–2.35)	0.595
TEHP	1.68 (0.68–4.78)	0.231	1.24 (0.50–3.09)	0.648	0.90 (0.40–1.90)	0.787	1.12 (0.36–3.53)	0.844
TBOEP	1.55 (0.59–4.09)	0.376	0.96 (0.49–1.87)	0.898	0.77 (0.46–1.30)	0.328	1.31 (0.59–2.88)	0.507
TDCIPP	1.82 (0.65–5.09)	0.254	1.01 (0.51–1.99)	0.987	0.89 (0.52–1.50)	0.653	1.47 (0.65–3.35)	0.358
TPHP	1.64 (0.60–4.85)	0.338	0.85 (0.42–1.68)	0.626	0.83 (0.48–1.43)	0.503	0.72 (0.31–1.66)	0.433
∑PFRs	2.00 (0.61–6.53)	0.251	0.95 (0.40–2.28)	0.915	0.94 (0.47–1.87)	0.854	1.03 (0.36–2.91)	0.962

CI, confidence interval; OR, odds ratio; PFRs, organophosphate esters; TBOEP, tris(2-butoxyethyl) phosphate; TNBP, tributyl phosphate; TCEP, tris(2-chloroethyl) phosphate; TCIPP, tris(2-chloro-*iso*-propyl) phosphate; TMPP, tricresyl phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TPHP, triphenyl phosphate; ∑PFR, sum of all measured organophosphate esters;
The odds ratios were calculated using $\log_{10}$-transformed variables
Each variable was modeled separately using a logistic regression model
Adjusted for gender, age, tobacco smoke or ETS exposure, renovation, wall-to-wall carpeting, dampness index, hair/fur-bearing pets in the dwelling, mechanical-ventilation equipment usage, and total fungi

Supporting Information

Table S1 GC-FPD analysis conditions

Component	Condition
Detector	Flame photometric detector (P-filter)
Column	DB-17, 30 m × 0.53 mm (i.d.) × 1 µm
Oven temperature	90°C (2 min); 15°C/min to 170°C; 5°C/min to 220°C; 20°C/min to 260°C (10 min)
Carrier gas	Helium, 20 ml/min (constant flow mode)
Make-up gas	Helium, 25 ml/min
Hydrogen flow	75 ml/min
Air flow	100 ml/min
Inlet temperature	250°C
Injection volume	2 µl, splitless mode (purge at 1 min)
Detector temperature	250°C

Table S2 Recovery rate and instrumental limit of detection of PFRs

PFR	Recovery rate (%; n = 3)	LOD[a] (pg)
TMP	95.7 ± 1.9	18.8
TEP	93.7 ± 1.0	7.6
TPP	94.8 ± 2.4	6.8
TNBP	95.2 ± 3.2	11.6
TCIPP	82.7 ± 9.7	27.2
TCEP	91.5 ± 8.0	19.2
TEHP	91.2 ± 9.3	16.8
TBOEP	91.9 ± 9.8	18.0
TDCIPP	88.5 ± 8.9	20.8
TPHP	96.3 ± 7.2	20.0
TMPP	91.8 ± 5.6	100

PFR, organophosphate ester; TMP, trimethyl phosphate; TEP, triethyl phosphate; TPP, tripropyl phosphate; TNBP, tributyl phosphate; TCIPP, tris(2-chloro-*iso*-propyl) phosphate; TCEP, tris(2-chloroethyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TBOEP, tris(2-butoxyethyl) phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TPHP, triphenyl phosphate; TMPP, tricresyl phosphate.

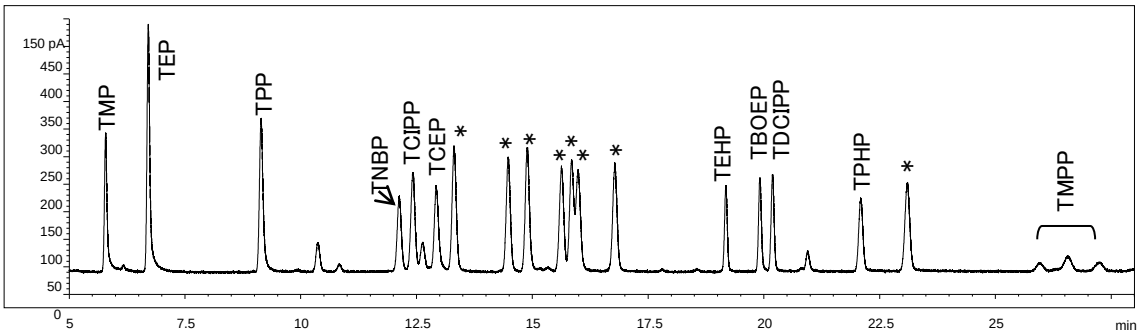
[a]LOD, Limit of detection (based on a signal-to-noise ratio of 3)

Table S3 Unadjusted models of relationships between asthma and allergies and PFRs and other environmental variables

	Asthma		Atopic dermatitis		Allergic rhinitis		Allergic conjunctivitis	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Floor (n = 494)								
TNBP	**2.27 (1.19–4.32)**	**0.013**	1.66 (1.00–2.76)	0.050	0.86 (0.54–1.38)	0.542	1.24 (0.67–2.29)	0.502
TCIPP	0.72 (0.33–1.56)	0.407	**1.73 (1.05–2.85)**	**0.032**	0.91 (0.61–1.36)	0.642	0.76 (0.41–1.39)	0.373
TCEP	0.96 (0.42–2.21)	0.927	1.62 (0.93–2.85)	0.088	1.22 (0.78–1.89)	0.387	1.09 (0.57–2.08)	0.805
TEHP	1.84 (0.70–4.81)	0.215	**2.31 (1.17–4.54)**	**0.016**	1.56 (0.92–2.65)	0.102	0.76 (0.34–1.71)	0.510
TBOEP	1.15 (0.59–2.26)	0.682	1.27 (0.79–2.05)	0.326	1.20 (0.83–1.73)	0.323	0.93 (0.55–1.56)	0.772
TDCIPP	1.70 (1.00–2.89)	0.052	**1.94 (1.33–2.84)**	**0.001**	0.97 (0.71–1.32)	0.826	1.53 (0.99–2.34)	0.053
TPHP	1.40 (0.56–3.47)	0.467	1.76 (0.94–3.29)	0.077	1.00 (0.60–1.68)	0.991	0.90 (0.42–1.93)	0.782
∑PFRs	1.24 (0.55-2.76)	0.605	1.57 (0.89-2.78)	0.119	1.20 (0.78-1.85)	0.414	0.88 (0.47-1.64)	0.681
Multi-surface (n = 390)								
TNBP	1.70 (0.63–4.56)	0.296	0.79 (0.36–1.75)	0.560	1.70 (0.94–3.05)	0.077	0.89 (0.35–2.22)	0.798
TCIPP	1.10 (0.47–2.58)	0.827	1.07 (0.59–1.94)	0.823	1.39 (0.86–2.25)	0.177	1.26 (0.62–2.53)	0.520
TCEP	1.08 (0.55–2.12)	0.828	1.12 (0.70–1.79)	0.640	1.27 (0.87–1.85)	0.211	1.19 (0.69–2.05)	0.536
TEHP	0.92 (0.28–2.97)	0.886	1.48 (0.69–3.14)	0.313	1.20 (0.64–2.25)	0.577	1.41 (0.58–3.43)	0.443
TBOEP	1.18 (0.55–2.51)	0.675	1.03 (0.61–1.76)	0.909	0.97 (0.64–1.49)	0.903	1.19 (0.64–2.23)	0.581
TDCIPP	1.60 (0.73–3.50)	0.241	1.21 (0.70–2.11)	0.498	1.07 (0.69–1.67)	0.761	1.58 (0.83–3.03)	0.163
TPHP	1.26 (0.58–2.74)	0.568	1.09 (0.63–1.89)	0.767	0.99 (0.63–1.54)	0.953	0.98 (0.51–1.89)	0.964
∑PFRs	1.15 (0.42-3.17)	0.780	0.98 (0.48-2.01)	0.959	1.03 (0.58-1.84)	0.910	0.99 (0.42-2.30)	0.976
Other environmental variables (n = 516)								
Formaldehyde	1.03 (0.22–4.85)	0.967	1.00 (0.45–2.92)	0.999	1.83 (0.78–4.27)	0.164	2.52 (0.72–8.87)	0.150
Total VOCs	0.42 (0.05–3.66)	0.434	0.89 (0.26–3.05)	0.847	0.49 (0.17–1.45)	0.197	0.28 (0.04–1.80)	0.178
Total fungi	0.57 (0.24–1.34)	0.193	**0.39 (0.22–0.72)**	**0.002**	0.73 (0.46–1.17)	0.193	0.36 (0.28–1.13)	0.104
Der1	0.95 (0.60–1.49)	0.803	0.94 (057–1.56)	0.943	0.97 (0.73–1.28)	0.837	1.07 (0.72–1.60)	0.731

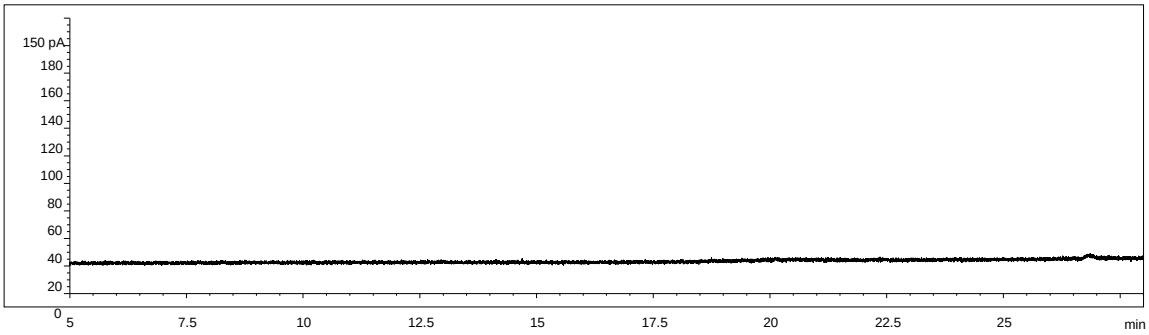
CI, confidence interval; PFRs, organophosphate esters; OR, odds ratio; TBOEP, tris(2-butoxyetyl) phosphate; TNBP, tributyl phosphate; TCEP, tris(2-chloroethyl) phosphate; TCIPP, tris(2-chloro-iso-propyl) phosphate; TMPP, tricresyl phosphate; TDCIPP, tris(1,3-dichloro-2-propyl) phosphate; TEHP, tris(2-ethylhexyl) phosphate; TPHP, triphenyl phosphate; ∑PFR, sum of all measured organophosphate esters; VOCs, volatile organic compounds
Der1: the sum of the values for Der p1 and Der f1
The odds ratios were calculated using $\log_{10}$-transformed variables
Each variable was modeled separately using a logistic regression model

Standard solution



*: Organophosphate pesticides

Blank (acetone)



Floor dust

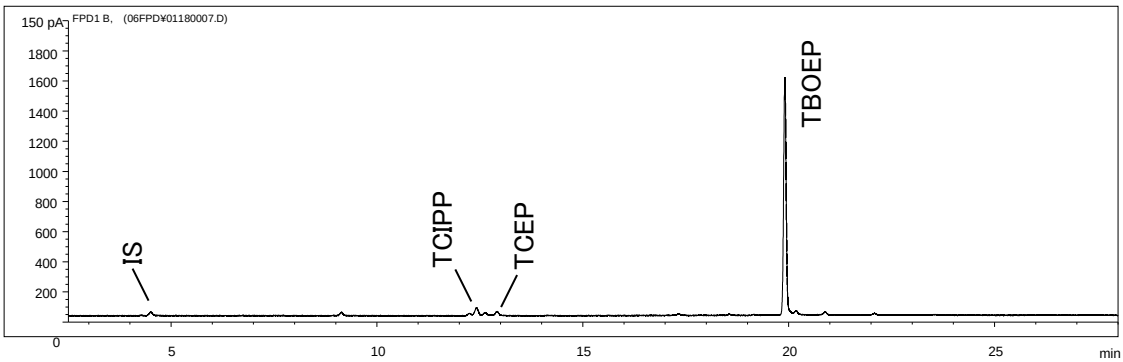


Fig. S1 Gas chromatogram of PFRs in the standard solution, an acetone blank, and an indoor floor dust sample

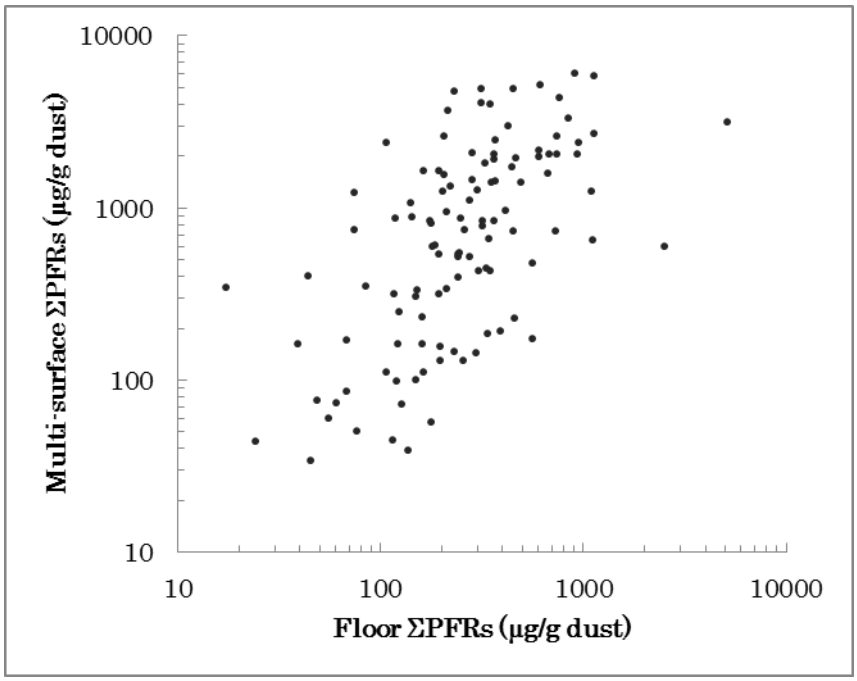


Fig. S2 Plot of concentrations of ΣPFRs in floor dust and multi-surface dust from 112 homes.